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CASE REPORT Open Access

Darier disease, hypertrophic / vegetating type

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Abstract

Background: A hypertrophic / vegetating variant of Darier disease causing massive verruciform genital tumors is exceedingly rare.

Case presentation: A woman in her late 50s underwent wide resection of vulva and inguinal skin due to massive verruciform lesion. She had crusted / keratotic plaques with appearance of follicular keratosis keratosis (with a greasy, warty texture) in the back, neck, face, and extremities for 27 years. Previous biopsies from lesions elsewhere 27 years ago and along the years showed the same verruciform, pseudoepitheliomatous pattern, with no atypia. The diagnosis in those biopsies as well in the resected specimen was Darier disease, hypertrophic / vegetating type. All sampled areas showed the same pattern of parakeratosis, dyskeratosis (corps ronds and grains), suprabasal acantholysis and pseudoepitheliomatous hyperplasia with prominent anastomosing cords of elongated rete ridges (with a syringofibroadenoma silhouette). HPV hybridization situ was negative.

Conclusion: Awareness of hypertrophic variant of Darier disease is of important to avoid the diagnosis of malignant transformation in long term disease – which is an exceedingly rare event.

Keywords: Vulva, Darier disease, Vulvar diseases

Background

A hypertrophic / vegetating variant of Darier disease causing massive verruciform genital tumors is exceedingly rare.

Case presentation

A woman in her late 50s underwent wide resection of vulva and inguinal skin due to massive verruciform lesion (Figs. 1 and 2). She had crusted / keratotic plaques with appearance of follicular keratosis with a greasy, warty texture in the back, neck, face, and extremities for 27 years.

Previous biopsies from lesions elsewhere 27 years ago and along the years showed the same verruciform, pseudoepitheliomatous pattern, with no atypia. The diagnosis in those biopsies as well in the resected specimen was Darier disease, hypertrophic / vegetating type. Extensive sampling showed no atypia and no invasive foci. All sampled areas showed the same pattern of parakeratosis, dyskeratosis (corps ronds and grains), suprabasal acantholysis and pseudoepitheliomatous hyperplasia with prominent anastomosing cords of elongated rete ridges (with a syringofibroadenoma silhouette) (Figs. 3 and 4). HPV hybridization situ was negative.

Discussion

Darier disease is caused by impaired keratinocyte adhesion caused by inactivating mutations of SERCA2 – a type 2 sarcoendoplasmic reticulum CA^{2+}-ATPase. Impaired imbalance of calcium intracellular homeostasis results in the characteristic apoptosis of keratinocytes. It is a rare disease that is usually transmitted in an

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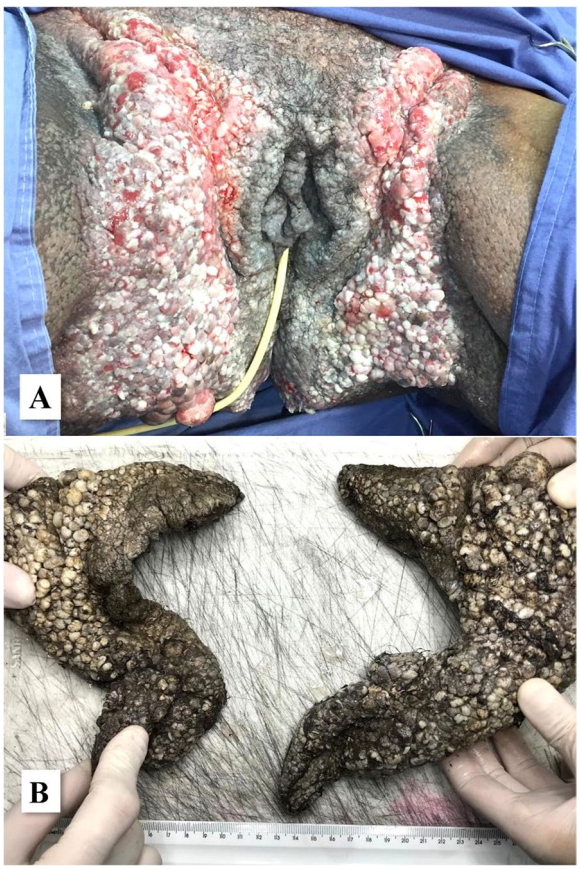

Fig. 1 Pre-operative photograph of a verruciform mass in vulva and inguinal skin (**A**). Formalin-fixed specimens (**B**)

autosomal dominant pattern. About 47% of all patients do not show a positive familial history and it has been explained by new mutations or incomplete penetrance. Disease presentation peaks at puberty, however, some patients may show signs of disease only by the sixth or seventh decades of life (Calonje et al. 2018).

Patients exhibit crusted and keratotic yellow-brown papules and plaques concentrated in "seborrheic" areas such as scalp', forehead, ears, nasolabial folds, upper chest, back and supraclavicular fossae. Lesions may be induced or exacerbated by stress, heat, or sweating; and are susceptible to bacterial, viral and fungal infections. Other characteristic forms of involvement are acrokeratosis verruciformis-like lesions in the back of the hands, white and red streaks in nails, and lesions in mucous membranes and genitalia (Calonje et al. 2018).

Apoptotic fragments result in typical features of dyskeratosis such as corps ronds (pyknotic nucleus surrounded by a clear halo and large keratohyalin bodies in granular layer) and grains (flattened cells with cigar-shaped nuclei in horny layer) (Calonje et al. 2018).

A rare form of Darier disease is the hypertrophic / vegetating variant (Aliağaoğlu et al. 2006; Pezzini et al. 2015). It was described in 1949 by Beerman and included a case of mass forming lesion in male genitalia (Beerman 1949). Other case has been described of extensive involvement in anogenital area (Ji et al. 2018).

Hailey-Hailey disease maybe considered in differential diagnosis due to the presence of lesions with verrucous appearances in inguinal and perineal areas. Both Darier disease and Hailey-Hailey disease are cornification associated conditions with mutations in genes coding for intracellular calcium pumps: caused by ATP2A2 and ATP2C1 gene mutations, respectively. Both are inherited as autosomal-dominant traits and show highly variable phenotype (Nellen et al. 2017). In the present case, the diagnosis of Darier disease is favored by the presence of less acantholysis as expected for Hailey-Hailey disease, more dyskeratosis, and clinical involvement of "seborrheic" areas such as scalp, face, upper chest, back. In addition, acantholytic zones involved adnexal structures (especially hair follicles) and numerous corps ronds and grains could be seen.

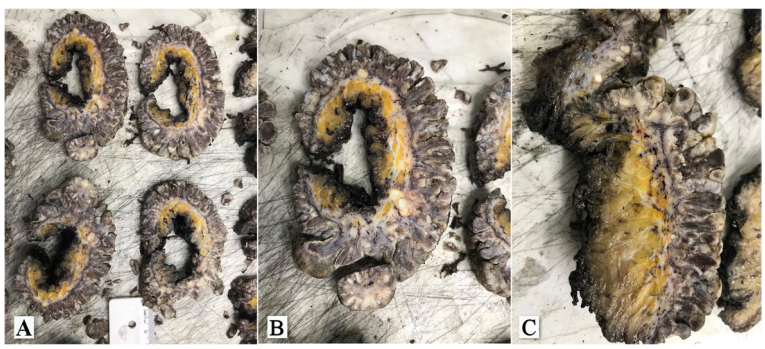

Fig. 2 Cut surface of the specimens

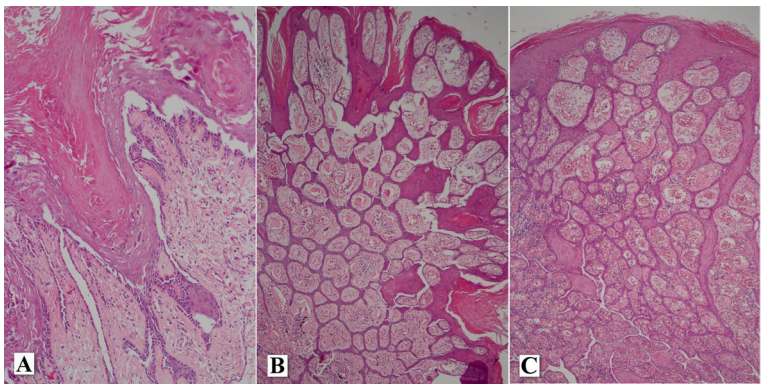

Fig. 3 Suprabasal acantholysis (**A**: HE, 100x) and pseudoepitheliomatous hyperplasia with prominent anastomosing cords of elongated rete ridges (with a syringofibroadenoma silhouette) (**B** and **C**: HE, 40x)

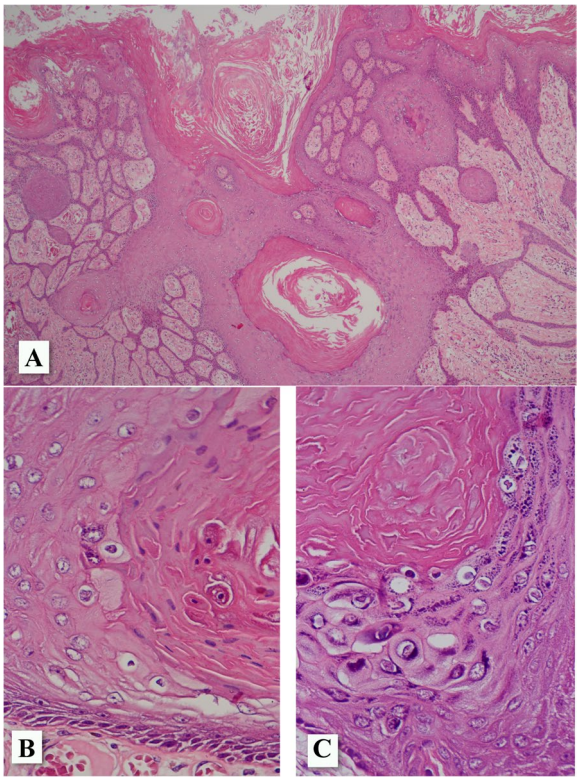

Fig. 4 Pseudoepitheliomatous hyperplasia with prominent anastomosing cords of elongated rete ridges (with a syringofibroadenoma silhouette) (**A**: HE, 40x). Grains (**B**: HE, 400x) and corps ronds (**C**: HE, 400x)

Conclusion

Awareness of hypertrophic variant of Darier disease is of important to avoid the diagnosis of malignant transformation in long term disease – which is an exceedingly rare event. The differential diagnosis with HPV associated lesions and other vulvar dermatosis are critical for the proper management.

Abbreviations

SERCA2: Sarco/endoplasmic reticulum Ca2 + —ATPase.

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None.

Authors' contributions

CPC and DAA conceived the idea. CPC and DAA was the major contributor to the writing of the manuscript. CPC and DAA diagnosed the cases. HUBA, NAV and FL were major contributors for critically revising the manuscript for important intellectual content. The authors read and approved the final manuscript.

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Availability of data and materials

Supplementary data is available upon request.

Declarations

Ethics approval and consent to participate

Ethics approval: this study was approved by the Ethics Committee of the Faculty of Medicine, Federal University of Bahia (approval number 5.521.203, year 2022).
Written informed consent was obtained from the patient for participation in this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
The authors declare that they have no competing interests.

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